Case report

Multiple symmetric lipomatosis type I in a female patient with neuropathy: no association with alcoholism or mitochondrial DNA m.8344A>G mutation

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Case report

A 69-year-old Caucasian HIV-negative woman presented to the Department of Dermatology at the Patras University Medical Center with a 3-year history of progressively enlarging disfiguring masses over the upper part of her body. She had no history or evidence of systemic infections, autoimmune or neoplastic disorders. Additionally, she had no history of alcohol abuse and her family history was unremarkable.

The patient presented with a height of 158 cm, a weight of 108 kg and a body mass index of 43.3. Physical examination revealed extremely large, painless and symmetrical subcutaneous masses on the neck, shoulders, proximal arms and axillae (Figure 1). She experienced no discomfort, dyspnea, dysphagia or dysphonia. Histological examination of the nonencapsulated masses showed a network of mature adipocytes without evidence of increased vascularity or malignancy. Based on these findings, the diagnosis of multiple symmetric lipomatosis (MSL) (type I) was established.

On clinical neurologic examination, there was a weakness of the proximal leg muscles (4/5 Medical Research Council score), whereas motion of the shoulder muscles was limited probably due to the fat deposits. Apart from ankle reflexes, all tendon reflexes were present and symmetrical. Pain and touch sense were moderately reduced in a stocking distribution up to the knee level bilaterally and normal in the upper limbs. Vibration sense and joint position were reduced distally to knee level in the lower limbs and to the fingers in the upper limbs. Motor conduction studies of the median, ulnar and fibular nerve were unremarkable. Sensory action potential (SAP) was normal in the median, of low amplitude in the ulnar and absent in the sural nerve. Sympathetic skin response was normal in the palm and unreliable in the sole. Taken together, the clinical and neurophysiological findings favored the diagnosis of a sensory neuropathy. Electromyography of biceps brachii, quadriceps and tibialis anterior muscles showed absence of spontaneous activity, motor unit potentials of normal configuration and full interference pattern on maximal voluntary activity. EEG was normal, whereas brain MRI revealed chronic ischemic infarcts in the left parietal–occipital lobe, lacunar infarcts in the basal ganglia bilaterally and cerebral atrophy. The Mini-Mental State Examination revealed difficulties of the patient’s recent memory (registration recall default), although

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the overall score 25/30 was at the lower normal limit.

Abdominal computer tomography showed formations of soft tissue density (3 cm in diameter) in the upper thoracic paraspondylar spaces. Routine laboratory tests revealed the following abnormal findings: decrease of serum calcium and of 24 h urine calcium, increase of serum cholesterol, immunoglobulin A and immunoglobulin E levels. During a 75 g oral glucose tolerance test, the patient was found to meet the criteria for diabetes mellitus. Hormonal investigations showed a slight increase of thyroid-stimulating hormone compatible with subclinical hypothyroidism, an increase of parathyroid hormone and a decrease of 25(OH) vitamin D consistent with the diagnosis of vitamin D deficiency with secondary hyperparathyroidism.

Molecular genetic analysis of extracted blood DNA for the m.8344A>G mitochondrial DNA (mtDNA) mutation revealed normal results, which essentially excluded the presence of this mtDNA mutation as the underlying cause of the patient’s symptoms. Since the patient refused a muscle biopsy, no histological, histochemical and molecular genetic investigations of muscle tissue could be performed. Additionally, she refused to undergo lipectomies, which were proposed as therapeutic approach to her disorder. We recommended further abstinence from alcohol and initiation of treatment for her newly diagnosed diabetes mellitus, hypercholesterolemia, hypothyroidism and vitamin D deficiency.

Discussion

MSL, also known as Madelung’s disease or Launois-Bensaude’s syndrome, is an uncommon disorder (incidence 1:25 000) characterized by symmetric and nonencapsulated fatty deposits mainly involving the neck, upper thorax and arms.1 MSL mostly affects men of Mediterranean origin between their third and sixth decades of life and occurs in two clinical types: in type I, lipomas are localized on the neck, shoulders and upper thorax, whereas in type II, they extend all over the body.2 MSL type I rarely occurs in women and data concerning the involvement of the nervous and endocrine–metabolic system in this type are sparse. Mechanisms possibly underlying the transformation of adipose tissue to lipomas include a defect in the catecholamine-stimulated lipolytic pathway leading to an excessive lipid accumulation,3 a sympathetic denervation of brown fat adipocytes resulting in their hypertrophy4,5 and mutations of mtDNA.6

The main neurological manifestation of the patient presented herein was a pure sensory, length-dependent peripheral neuropathy affecting the lower and upper limbs. The abnormal SAPs indicated a definite involvement of large diameter-myelinated sensory fibers, whereas no unequivocal signs of dysfunction of small diameter-unmyelinated sensory fibers existed. Neuropathy is a common feature of MSL, which occurs in 76–84% of the patients and is usually referred to as a combined motor and sensory and less frequently autonomic neuropathy.6–8 Only three patients, all of them being males, have been reported with pure sensory neuropathy, which was confirmed by neurophysiology in one case.6,8–11

In our case, alcoholism or other known cause of neuropathy in this disorder was not found. The newly diagnosed diabetes mellitus might be the obvious cause of neuropathy in our patient; however, this possibility seems very unlikely in view of the absence of motor involvement and of autonomic sweating abnormality12 and of the fact that neuropathy was disproportionally more severe than that expected in a case of impaired glucose tolerance.13 Alternatively, the neurological findings in our patient could be attributed to the subclinical hypothyroidism.14

The etiology of MSL seems to be heterogeneous, with some cases being associated with mtDNA mutation and some others, sporadic, lacking any genetic background. The only genetic basis identified to date is mtDNA mutation, particularly m.8344A>G, that is often referred to as the myoclonic epilepsy and ragged-red fibers (MERRF) mutation, as it was first reported in association with MERRF syndrome.4–6 There are only a few case/family reports of MSL associated with m.8344A>G.9–11 MSL has also been reported in individuals from at least two families with the m.8363A>G mtDNA mutation, a rare cause of MERRF syndrome; interestingly, these patients had also other manifestations of mitochondrial disease.15 mtDNA mutation may account for the majority of MSL cases without a history of alcoholism; for example, Klopstock et al.16 identified mtDNA mutation in 2/3 patients without a history of alcoholism, but in none of 14 patients with high

Figure 1. Anterior (A) and lateral view of the patient (B).
alcohol intake. Although in the case reported here, the presence of m.8344A>G was excluded, the patient's MSL, peripheral sensory neuropathy and diabetes mellitus could be attributed to an underlying mitochondrial genetic abnormality, which could not be further investigated since a muscle biopsy was refused by the patient.

Conflict of interest: None declared.

References